Should echocardiography be performed in all acute ischemic stroke patients? Echocardiography in acute ischemic stroke

Echocardiography in acute ischemic stroke

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Abstract

Aim: Echocardiography is one of the most commonly used diagnostic methods in the investigation of cardiac etiologies among patients with acute ischemic stroke (AIS). However, data regarding the diagnostic value of this method in patients with and without cardiac abnormalities are limited. The aim of this study is to determine the diagnostic yield of echocardiography in AIS patients with and without any cardiac disease.

Material and Methods: We retrospectively analyzed the data of patients with an AIS regarding medical history, cardiac examination, transthoracic echocardiography and transesophageal echocardiography. The patients were divided into two groups. Patients with a history of cardiac disease, cardiovascular risk factors, and abnormal findings in cardiac examination or ECG were allocated into Group A, while Group B included patients without cardiac disease with ischemic stroke.

Results: A total of 633 patients with acute ischemic stroke (327 females (51.7%); mean age: 68.9±13.4 years) were included in the study. There were 393 patients in Group A (62.1%), and 240 patients in Group B (39.9%). The diagnostic yield of echocardiography was significantly more frequent in Group A (41.2%) than in Group B (28.3%) (p=0.001). Antithrombotic treatment was changed among 24 (6.1%) patients in Group A and 19 (7.9%) patients in Group B as a result of the echocardiography findings (p=0.38).

Discussion: The diagnostic yield of echocardiography is low if it is used routinely in patients with acute ischemic stroke. Consequently, echocardiography could be performed for acute ischemic stroke patients with negative diagnostic work-up for other etiologic stroke subtypes

Keywords

Diagnostic Yield, Echocardiography, Ischemic Stroke

Introduction

Ischemic stroke is a heterogeneous disease with different mechanisms and etiologies [1]. Determination of the underlying etiological factor is essential to prepare an adequate preventive strategy [2].

Up to 15-30% of ischemic strokes are caused by cardiac sources of embolism [3,4]. Diagnosis of a potential source of cardiac embolism may be performed using 12-lead standard electrocardiography (ECG), cardiac rhythm monitoring at least 24-48 hours, and transthoracic echocardiography (TTE) and/or transesophageal echocardiography (TEE) [5-7].

Echocardiography is the most commonly used diagnostic method for the detection of cardiac sources among patients with ischemic stroke. The European Stroke Organization guidelines recommend the use of echocardiography in selected patients while the American Stroke Association guidelines do not make any clear recommendation on the use of echocardiography [8]. In a study by Abreu et al., TTE was performed in all ischemic stroke patients with normal sinus rhythm [9]. Otherwise, some of the previous studies have reported that TTE and TEE should not be performed in all ischemic stroke patients, but they could be performed for only selected patients, such as no clear stroke etiology or younger patients [10-12].

The aim of this study is to determine patient characteristics that may increase the diagnostic value of echocardiography in ischemic stroke patients with and without any history of cardiac disease or risk factor in medical history and abnormal findings in cardiac examination or electrocardiography.

Material and Methods

Patients

The medical records of 633 consecutive patients who were admitted with acute ischemic stroke were retrospectively evaluated. Prior to the study, approval was obtained from the research ethics committee. The patients were divided into two subgroups: Group A included patients with any history of cardiac disease or cardiovascular risk factor and abnormal findings in cardiac examination or electrocardiography, while Group B included the patients with controlled hypertension and other remaining patients.

Patient demographics and cardiovascular risk factors, including history of hypertension, atrial fibrillation, congestive heart failure, coronary artery disease at admission were collected using a standard data collection form and entered into an institutional database. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg on repeated measurements or prior use of antihypertensive medication, atrial fibrillation, defined by the presence in the medical history or detection on ECG or Holter. Controlled hypertension was defined as systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg with antihypertensive drug treatment. The definition of controlled hypertension was then confirmed by ambulatory blood pressure monitoring or hospital observation forms. Coronary artery disease was defined as any presentation with angina pectoris, the existence of ischemic ECG changes, myocardial infarction suggested by pathological Q waves on ECG or confirmed by medical records, any history of coronary revascularization, or presence of coronary artery stenosis ≥ 50% in coronary angiogram or any history of coronary revascularization by percutaneous coronary intervention or coronary artery by-pass graft operation. Congestive heart failure was defined as the presence of symptoms such as dyspnea at rest or on exercise, fatigue and peripheral edema, along with structural heart disease, as confirmed by echocardiography or elevated natriuretic peptides. Abnormal findings of physical examination included distended jugular veins, thrill on palpation of precordium, presence of S3 or S4 gallop, any diastolic murmur or more than Levine 2/6 systolic murmur, crackles heard on lung fields, hepatomegaly, splenomegaly, ascites and extremity edema.

A single rater (MHS) determined etiologic stroke subtypes using the automated Causative Classification System (CCS, available at https://ccs.mgh.harvard.edu) [13]. The CCS subtypes included supra-aortic large artery atherosclerosis, cardio-aortic embolism, small artery occlusion, other causes, and undetermined causes. Etiologic work-up included vascular imaging studies, such as carotid Doppler ultrasonography, computerized tomography angiography, magnetic resonance angiography or digital subtraction angiography, TTE or TEE, 24-hour cardiac rhythm monitoring, and laboratory tests for hypercoagulability and vasculitis.

Cardiological Evaluation

Transthoracic and transesophageal echocardiographic examinations were performed using the Vingmed System 7 (Vivid 7; GE, Horten, Norway), according to the recommendations of the American Society of Echocardiography [14]. Patent foramen ovale (PFO) was considered by the appearance of microbubbles in the left atrial after intravenous injection of agitated saline, spontaneously or after the Valsalva maneuver, within 3 cardiac cycles and complete opacification of right atrium. Atrial septal aneurysm was defined as hypermobile thin-walled septum primum in the region of the fossa ovalis with a base at least 1.5 cm and an excursion during the cardiac cycle at least 1.5 cm [15]. Complex thoracic aortic atheroma was classified as mobile plaques or plaques protruding 4 mm or more into the lumen and/ or plaques with ulceration [16].

The diagnostic yield of echocardiography was defined as the detection of cardiac sources of embolism (high risk, low risk or uncertain risk for CCS) excluding patients with AF or paroxysmal AF. The diagnostic yield was considered to be the number of patients who had at least one cardiac source of embolism.

Statistics

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 16.0 version (SPSS Inc. Chicago, Illinois, USA). Descriptive statistics were expressed as means/standard deviations for normally distributed continuous variables and median/interquartile range for variable with skewed distribution. Statistical analysis was performed to determine the diagnostic value of echocardiography in patients with ischemic stroke. The group rates were compared using a chi-squared test, and the means were compared using Student's t-test; $p<0.05$ was considered to be statistically significant.

Results

A total of 633 patients with acute ischemic stroke (306 males

Table 1. Epidemiologic and clinical characteristics of patients in Group A and Group B

	Group A	Group B	P
	n=393	n=240	
Age, year, Mean±SD	71.1±11.8	65.4±15.1	<0.001
Sex, n(%)			
Female	209(63.9)	118(36.1)	0.33
Male	184(60.1)	122(39.9)	
Medical history			
- Hypertension, n(%)	323 (82.2)	142(59.2)	
- Atrial fibrillation, n(%)	128(32.6)		
- CAD, n(%)	171(43.5)		<0.001
- CHF, n(%)	62(15.8)		
- Valve replacement	10 (2.5)		
Atrial fibrillation, n(%)			
- ECG	191(30.2)		<0.001
- Holter	45(11.5)	30(12.5)	
Transthoracic echocardiography, n(%)	391(99.5)	239(99.6)	0.87
Transesophageal echocardiography, n(%)	55(14)	29(12.1)	0.49

SD: Standard Deviation, CAD: Coronary Artery Disease, CHF: Congestive heart failure, PFO: Patent foramen ovale

Table 2. Echocardiographic findings of patients in Group A and Group B

Echocardiography findings, n(%)	Group A	Group B	P
	(n=393)	(n=240)	
TTE, n(%)			
- left atrium dilation	161 (41.2)	61 (25.5)	<0.001
- mitral stenosis	15 (3.8)	8 (3.3)	0.19
- aortic stenosis	15 (3.8)	2 (0.8)	0.001
- endocarditis	10 (2.6)	5 (2.1)	0.006
- left ventricular thrombus	50 (12.8)	9 (3.8)	<0.001
- left ventricle dysfunction	71 (18.2)	12 (5)	<0.001
- left ventricle aneurysm	18 (4.6)	7 (2.9)	0.004
- ejection fraction < 30%	48 (12.3)	7 (2.9)	<0.001
- spontaneous echo contrast	19 (6.1)	3 (2.0)	0.12
- interatrial septum aneurysm	13 (4.4)	14 (9.5)	0.101
- PFO	20 (6.6)	13 (8.3)	0.85
- vegetation	13 (4.3)	15 (9.8)	0.027
TEE			
- left atrium dilation	26 (47.3)	9 (31)	0.13
- mitral stenosis	1 (1.8)	1 (3.4)	0.19
- aortic stenosis	2 (3.6)	0 (0)	0.14
- endocarditis	1 (1.8)	0 (0)	0.18
- left ventricular thrombus	2 (3.6)	0 (0)	0.14
- left ventricle dysfunction	13 (23.6)	2 (6.9)	0.054
- left ventricle aneurysm	4 (7.3)	1 (3.4)	0.19
- ejection fraction < 30%	4 (7.3)	0 (0)	0.09
- spontaneous echo contrast	18 (32.7)	3 (10.7)	0.034
- atrial thrombus	13 (24.1)	7 (23.2)	0.95
- atrial myxoma	1 (1.9)	0 (0)	0.46
- interatrial septum aneurysm	7 (13.2)	2 (7.1)	0.409
- PFO	8 (14.8)	8 (27.6)	0.16
- atheroma in the ascendant aorta	4 (7.4)	7 (25.0)	0.027
- vegetation	4 (7.5)	5 (17.2)	0.15
Abnormal echocardiography finding, n(%)	379 (96.4)	98 (41)	<0.001
Diagnostic yield, n(%)	162 (41.2)	68 (28.3)	0.001

SD: Standard Deviation, TTE: transthoracic echocardiography, TEE: transesophageal echocardiography, PFO: Patent foramen ovale

Table 3. Etiologic stroke subtypes of patients in Group A and Group B

	Group A	Group B	P
	n=393	n=240	
CCS classification, n(%)			
- Large-artery atherosclerosis	81 (20.6)	69 (28.8)	0.02
- Cardioembolism	203 (51.7)	75 (31.2)	0.006
Cardioembolism-evident-probable	170 (83.7)	30 (40)	
Cardioembolism-possible	33 (16.3)	45 (60)	
- Small artery occlusion	15 (3.8)	10 (4.2)	0.83
- Other rare causes	3 (0.8)	24 (10)	<0.001
- Undetermined causes	91 (23.2)	62 (25.8)	0.38

CCS: Causative Classification System

(48.3%) and 327 females (51.7%); mean age: 68.9±13.4 (23-98) years) were included in the study. Patient demographics and medical risk factors are shown in Table 1. TTE was performed in 630 (99.5%) patients, and TEE was performed in 84 (13.3%) patients. Atrial fibrillation was detected in 191 (30.2%) patients using ECG.

There were 393 patients in Group A (62.1%) and 240 patients in Group B (39.9%). Atrial fibrillation was detected in 45 (11.5%) patients in Group A and 30 (12.4%) in Group B by using Holter. TTE and TEE findings in both groups are shown in Table 2. Left atrium dilation, aortic stenosis, endocarditis, thrombus in the left ventricle, left ventricle dysfunction, left ventricle aneurysm, ejection fraction < 30% and vegetation were more frequent in Group A, other vegetation and atheroma in the ascendant aorta were more frequent in Group B (Table 2). The diagnostic yield of echocardiography was significantly more frequent in Group A (n=162, 41.2%) than in Group B (n=68, 28.3%) (p=0.001).

Antithrombotic treatment was altered in 43 (6.8%) patients as a result of the echocardiography [24 patients (6.1%) vs 19 patients (7.9%) in groups A and B, respectively, p=0.38]. There was no significant difference in changing treatment between Group A and Group B.

The etiological stroke subtypes are shown in Table 3. Cardio-aortic embolism was more common in Group A compared to Group B (p<0.001). Evident and probable cardio-aortic embolism was 83.7% in Group A and 25.3% in Group B (Table 3).

Discussion

Cardiac sources of embolism are segregated into high- and low-risk categories with reference to an objective 2% primary stroke risk threshold [1]. Cardiac sources with a high primary risk of stroke are left atrial thrombus, left ventricular thrombus, atrial fibrillation, paroxysmal atrial fibrillation, sick sinus syndrome, atrial flutter, recent myocardial infarction, rheumatic mitral or aortic valve disease, bio-prosthetic and mechanical heart valves, low ejection fraction <28%, symptomatic heart failure with ejection fraction <30%, non-ischemic dilated cardiomyopathy, nonbacterial thrombotic endocarditis, infective endocarditis, papillary fibroelastoma and left atrial myxoma. Cardiac sources with a low primary risk of stroke are mitral annular calcification, patent foramen ovale, atrial septal aneurysm, atrial septal aneurysm with patent foramen ovale, left ventricular aneurysm without thrombus, isolated left atrial smoke, complex atheroma in the ascending aorta or proximal

arch and others (third-degree atrioventricular block, pre-excitation syndromes, etc.) in CCS [13[.

In our study, cardio-aortic embolic etiology was detected in 203 (51.7%) patients in Group A and 75 (31.2%) patients in Group B. Cardio-aortic embolic etiology was more common in Group A compared to Group B (p<0.001). High cardiac sources of embolism were more frequent in Group A, nevertheless, low cardiac sources of embolism were more frequent in Group B.

AF has been reported as the most common cause of embolic stroke [17]. Paroxysmal AF (PAF) is assumed to play also a dominant role in the pathogenesis of cryptogenic stroke [18]. PAF cannot be detected by standard ECG. Thus, it may be detected by a cardiac rhythm monitoring for at least 24 hours [19,20]. Gladstone et al. reported that they detected atrial fibrillation in one in six patients with ambulatory ECG monitoring for a target of 30 days. It was superior to an additional round of 24-hour ECG monitoring and clinical follow-up [21]. In this study, ECG detected AF in 191 (30.2%) patients in the Group A. AF was found in 45 (11.5%) patients in Group A and 30 (12.4%) in Group B by using Holter.

Other causes of evident and probable cardiac embolism and possible cardiac embolism could be diagnosed using TTE or TEE [8,9,22]. TTE is easier to perform, non-invasive, widely available and cheaper than TEE. However, it is clearly less sensitive for the detection of unknown cardiac sources of emboli [20]. The disadvantages of TEE are that it is semi-invasive, more expensive, and requires more experience to be perform adequately. TEE is more sensitive than TTE for detecting atrial septal aneurysm and defect, patent foramen ovale, atrial myxoma, atrial thrombus, atrial appendage thrombus, aortic arch atheroma, and mitral valve vegetations [6]. Atherosclerotic plaque thickness >4 mm within the aorta has been associated with a high risk of aorto-embolic ischemic stroke [23].

In some previous studies, only TTE was used to determine the causes of evident and probable cardiac embolism and possible cardiac embolism [9,24]. However, TEE combined with TTE was performed for the detection of cardiac sources in patients with ischemic stroke in some other studies [10-12]. In our study, TTE was performed in 630 (99.5%) patients, and TEE was performed in 84 (13.3%) patients.

After exclusion of patients with AF, common cardiac anomalies associated with ischemic stroke were dilated cardiomyopathy and severe heart failure following previous anterior wall myocardial infarction, left ventricular systolic dysfunction with an ejection fraction <35%, mitral valve stenosis with enlarged left atria, intracardiac masses, and valvular prosthesis determined by use of TTE [9,23]. In addition, PFO was the most common low-risk in potential source of cardiogenic embolism with ischemic stroke in most of previous studies which were examined by TEE [10,11]. Other cardiac anomalies were complex aortic plaques, atrial septal aneurysm and defect, atrial myxoma, atrial thrombus, and mitral valve vegetation in TEE [5,16].

In our study, left atrium dilation was the most common cardiac abnormality in both groups as measured byTTE and TEE. Other cardiac anomalies such as aortic stenosis, endocarditis, thrombus in the left ventricle, left ventricular dysfunction, left ventricular aneurysm, left ventricular ejection fraction < 30%

and vegetation were more frequent in Group A according to TTE findings, otherwise vegetation and atheroma in the ascendant aorta were more frequent in Group B according to TEE findings (p<0.05). Total abnormal TTE and TEE findings were significantly more frequent in Group A (96.4%) than in Group B (41%) (p<0.001), and the diagnostic yield of echocardiography was significantly more frequent in Group A (41.2%) than in the Group B (28.3%) (p=0.001). Cardio-aortic embolism was more common in Group A compared to Group B (p<0.001). Previous studies have not compared diagnostic value of echocardiography in ischemic stroke patients with and without any cardiac disease or risk factor in medical history and abnormal findings in cardiac examination or electrocardiography. Only Cho et al. retrospectively evaluated 3112 consecutive patients with ischemic stroke who had normal sinus rhythm and no history of cardiac disease, but did not compare to other patients with a history of cardiac disease [12].

Anticoagulation therapy was indicated in 0-37.2 % of ischemic stroke cases after examination with TTE or/and TEE in ischemic stroke patients [25]. The therapeutic impact of echocardiography in previous studies has varied widely due to different methods [14,26]. We found that antithrombotic treatment was changed in 43 patients as a result of the echocardiography findings. There were no significant differences in changing treatment between Group A and Group B.

There are several limitations in our study, including its retrospective design and relatively short follow-up duration. In addition, this is a restriction of the cohort of a single medical center. However, all of our patients underwent a detailed work-up for determining the causative mechanism of ischemic stroke. Acute ischemic lesions were identified with diffusion-weighted imaging in all patients. In contrast to the previous studies, the etiologic subtypes of all patients with acute ischemic stroke have been determined systematically according to the CCS in our patients.

Conclusion

The diagnostic yield of echocardiography is low if it is used routinely in acute ischemic patients. Otherwise, there was no significant difference in changing treatment between Group A and Group B. Thus, echocardiography could be performed for acute ischemic stroke patients with negative diagnostic work-up for other etiologic stroke subtypes.

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